probes. Viral DNA sequence was confirmed by PCR amplification of the polymerase catalytic region using the sense primer 5'-GCC TCA TTT TGT GGG TCA CCA TA-3' (SEQ ID NO: 1), (nucleotide 1408 to 1430 according to HBV Genebank Accession number M38454) and the antisense primer 5'-TCT CTG ACA TAC TTT CCA AT-3' (SEQ ID NO.: 2) (nucleotides 2817 to 2798 according to HBV Genebank Accession number M38454). The following primers were utilized for the sequencing of internal regions 5'-TGC ACG ATT CCT GCT CAA-3' (SEQ ID NO: 3) (nucleotides 2345-2362 according to HBV Genebank Accession number M38454) and 5'-TTT CTC AAA GGT GGA GAC AG-3' (SEQ ID NO: 4) (nucleotides 1790-1810 according to HBV Genbank Accession number M38454).--

## REMARKS

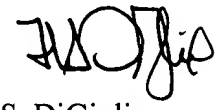
In response to the Notice to Comply dated November 30, 2001 and in accordance with the provisions in 37 C.F.R. §§1.821-§1.825, Applicants submit herewith a substitute paper and substitute computer readable copy of the Sequence Listing, along with a Statement Under 37 C.F.R. §1.821(f), stating that these copies are identical. A copy of the Notice to Comply is also enclosed.

By way of the substitute Sequence Listing, Applicants have further delineated the artificial sequences as set forth in SEQ ID NOS: 5-7 as reference HBV formula I, formula II and formula III, respectively. Support for these delineations is found in the specification at page 17, lines 18-21; page 26, lines 14-15; and page 33, lines 19-21. In addition, Applicants have further delineated the artificial sequences as set forth in SEQ ID NOS: 1-2 as primers. Support for these delineations is found at page 43, lines 27-29.

Furthermore, the specification has been amended to insert the sequence identifiers. No new matter has been introduced by such amendment. Attached hereto is a marked-up version of the changes made to the specification by the instant amendment. The attached page is captioned "**Version with Markings to Show Changes Made.**"

In view of the foregoing Amendment and the Remarks, it is believed that the subject case is in condition for an examination on the merits, which action is earnestly solicited.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE SPECIFICATION:**

Please amend the paragraph beginning at page 9, line 8 as follows:

--Figure 2 is a representation of the amino acid consensus sequence (SEQ ID NO: 8) from HBV DNA polymerase proteins encompassing regions which are conserved in the RNA polymerase protein. These regions are shown as domains A-E and are underlined. In the consensus sequence the M in the YMDD motif is designated as amino acid number 550. The amino acids which are subject to mutation during 3TC and/or FCV treatment are shown in bold. An asterisk (*) indicates greater than three amino acid possibilities at this position of the consensus sequence. The HbsAg major hydrophilic region containing the neutralization domain is indicated by a double line and the polymerase mutations which alter the HbsAg are indicated in italics.--

Please amend the paragraph beginning at page 9, line 18 as follows:

--Figure 3 is a representation of the nucleotide [sequence] sequences (SEQ ID NOS: 9-20) from various strains of HBV encoding the surface antigen. The amino acid sequence of the surface antigen beginning at amino acid 108 is shown above the nucleotide sequence.--

Please amend the paragraph beginning at page 9, line 28 as follows:

--Figure 5A is the representation of the nucleotide sequence (SEQ ID NO: 21) of HBV 1.28 genome.--

Please amend the paragraph beginning at page 9, line 30 as follows:

--Figure 5B is the representation of the nucleotide sequence (SEQ ID NO: 22) of HBV 1.5 genome.--

Please amend the paragraph beginning at page 17, line 18 as follows:

--The present invention extends to assaying any HBV mutant carrying a single or multiple substitution, addition and/or deletion or truncation in the amino acid sequence of the catalytic region of the HBV DNA polymerase as compared to the amino acid sequence set forth in Formula I (SEQ ID NO: 5) which is considered herein to define a reference HBV:--

Please amend the paragraph beginning at page 26, line 14 as follows:

--The amino acid sequence of an HBsAg and which is considered to define a reference HBV is set forth below in Formula II (SEQ ID NO: 6):--

Please amend the paragraph beginning at page 33, line 19 as follows:

--The altered HBsAg molecules of the HBV variants of the present invention may also be defined at the nucleotide level. The nucleotide sequence encoding the HBsAg from a reference HBV is set forth below in Formula III (SEQ ID NO: 7):--

Please amend the paragraph beginning at page 43, line 15 as follows:

--Purified recombinant transfer vector and linear AcMNPV baculovirus DNA were co-transfected into Sf21 cells using the BacNBlue transfection kit from Invitrogen (Carlsbad, CA); recombinant viruses were isolated by plaque assay according to the manufacturer's instructions. A series of recombinant viruses were amplified from isolated plaques by infecting 100-mm dishes of Sf21 cells. Viral DNA was extracted from amplified viruses using standard procedures. Purified viral DNA was digested with restriction enzymes and then fractionated by electropyhoresis in a 1.0% v/v agarose gel. Southern blotting was performed to determine which

virus isolates contained the intact 1.28, 1.5 or 1.3 HBV construct. A Boehringer Mannheim Random Prime DNA Labeling kit (Indianapolis, IN) was used to generate [$P^{32}$]-radiolabeled probes. A full-length double-stranded HBV genome was used as a template for all radiolabeled probes. Viral DNA sequence was confirmed by PCR amplification of the polymerase catalytic region using the sense primer 5'-GCC TCA TTT TGT GGG TCA CCA TA-3' [[<400>1]](SEQ ID NO: 1), (nucleotide 1408 to 1430 according to HBV Genebank Accession number M38454) and the antisense primer 5'-TCT CTG ACA TAC TTT CCA AT-3' [[<400>2]](SEQ ID NO.: 2) (nucleotides 2817 to 2798 according to HBV Genebank Accession number M38454). The following primers were utilized for the sequencing of internal regions 5'-TGC ACG ATT CCT GCT CAA-3' [[<400>3]](SEQ ID NO: 3) (nucleotides 2345-2362 according to HBV [Genbank]Genebank Accession number M38454) and 5'-TTT CTC AAA GGT GGA GAC AG-3' [[<400>4]](SEQ ID NO: 4) (nucleotides 1790-1810 according to HBV Genbank Accession number M38454).--